Inventors: Lockwood et al. Appl. Ser. No.: 10/629,538 Atty. Dkt.: 5777-00201

In the Specification:

Listed below is a marked-up copy of amended paragraphs of the Specification indicating the amended paragraphs of the Specification.

On page 14 of the previously submitted "Substitute Clean Specification", please amend the paragraph beginning on line 19 as follows:

FIG. 11A – FIG. 11C depicts an illustration of right-handed chiral arrangements of two *meso*-carotenoid molecules for which excitonic interactions produce long-wavelength positive and short-wavelength negative Cotton effects in the CD spectrum. Gray-colored molecules lie behind the plane of the paper.

On page 15 of the previously submitted "Substitute Clean Specification", please amend the paragraph beginning on line 3 as follows:

FIG. 14A – FIG. 14F depicts that the statistical mixture of stereoisomers of the disodium salt disuccinate astaxanthin derivative ("rac" in Figure Legends) induces functional gap junctional communication in murine embryonic fibroblast (10T1/2) cells. Confluent cultures were treated for 4 days as described in text, then assayed for the ability to transfer the fluorescent dye Lucifer Yellow. Arrows indicate the cell injected with Lucifer Yellow.

On page 16 of the previously submitted "Substitute Clean Specification", please amend the paragraph beginning on line 17 as follows:

FIG. 16A – FIG. 16F depicts that the statistical mixture of stereoisomers of the disodium salt disuccinate astaxanthin derivative increases the assembly of Cx43 immunoreactive junctional plaques. Confluent cultures of 10T1/2 cells were treated for 4 days as described above with the statistical mixture of stereoisomers of the disodium salt

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disuccinate astaxanthin derivative: (1) at 10⁻⁵M in 1:2 EtOH/ H₂O; (2) with 1:2 EtOH/ H₂O as solvent only negative control; or (3) TTNPB at 10⁻⁸M in tetrahydrofuran (THF) solvent as positive control. Cells were immunostained with a Cx43 antibody as described in text. FIG. 16Panel-A: the statistical mixture of stereoisomers of the disodium salt disuccinate astaxanthin derivative at 10⁻⁵M in 1:2 EtOH/ H₂O; FIG. 16Panel-C: 1:2 EtOH/ H₂O as solvent control; FIG. 16Panel-E: TTNPB at 10⁻⁸M in tetrahydrofuran (THF) solvent as positive control. FIGS. 16Panels-B, D, and F: digital analysis of FIGS. 16Panels-A, C, and E, respectively, demonstrating pixels above a fixed set threshold positive for fluorescent intensity. Light gray arrows: immunoreactive junctional plaques; dark gray arrows: position of cell nuclei. Note the greater number and intensity of junctional immunoreactive plaques in the cultures treated with the statistical mixture of stereoisomers of the disodium salt disuccinate astaxanthin derivative in comparison with solvent-only treated controls. The junctional plaques shown in FIGS. 16Panels-C and D represent infrequent plaques seen in controls; most cells in these cultures were negative for Cx43 staining.

On page 20 of the previously submitted "Substitute Clean Specification", please amend the paragraph beginning on line 22 as follows:

FIG. 35A - FIG. 35C depicts a comparison of an astaxanthin-treated dish to control dishes (see description for FIG. 34).

Please amend the Abstract as follows:

A method for inhibiting and/or ameliorating the occurrence of diseases associated with reactive oxygen species, reactive nitrogen species, radicals and/or non-radicals in a subject whereby a subject is administered a carotenoid structural analog, either alone or in combination with another carotenoid analog, or co-antioxidant formulation. The analog or analog combination is administered such that the subject's risk of experiencing diseases associated with reactive oxygen species, reactive nitrogen species, radicals

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and/or non-radicals may be thereby reduced. The analog or analog combination may be administered to a subject for the inhibition and/or amelioration of ischemia-reperfusion injury. The analog or analog combination may be administered to a subject for the inhibition and/or amelioration of, liver disease. The analog or analog combination may be administered to a subject for the inhibition and/or amelioration, of cancer. The analog or analog combination may be administered to a subject for the inhibition and/or amelioration of, cardiac arrhythmia and/or sudden cardiac death, and/or. The analog or analog combination may be administered to a subject for the inhibition and/or amelioration of any disease that involves production of reactive oxygen species, reactive nitrogen species, radicals and/or non-radicals. In one embodiment, a water-soluble and/or water-dispersible astaxanthin analog is particularly effective. This invention further includes pharmaceutical compositions comprising structural carotenoid analogs either alone or in combination.